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SOME PROBLEMS AND METHODS OF DIAGNOSIS OF CRETINISM AND JUVENILE HYPOTHYROIDISM*

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THE CLASSICAL PICTURE OF CRETINISM

The untreated cretin of more than two or three years usually presents a picture which is well known and easily recognized (Slide 1). The patient is dull, listless and apathetic. The body is short and stocky. The cretinoid facies is characterized by coarse, heavy features; small widely-spaced pig-like eyes with puffy lids; a broad, short nose with undeveloped bridge; a broad mouth with thick lips, broad protruded tongue. The skin is dry, thick, wrinkled, cool and shows circulatory mottling. The cheeks are pale, and may have a yellowish tinge due to carotene. The lips are pale and slightly dusky. The hair is sparse, coarse and dry.

THE USUAL TYPE OF CRETIN SEEN

The diagnosis is usually not so easy in the first year or two of life, because the cretin frequently does not present this characteristic appearance. (Slide 2). On superficial inspection, he might be mistaken for a fairly normal infant, considerably younger than his actual age. For example, this cretin of 12 months looks and acts like an infant of 5 or 6 months. This is due to the fact that the absence of thyroid activity causes a retardation in all the developmental processes;—growth, osseous development, dentition, and mental development. The study of the infant's level of development, particularly the osseous development, is a most essential procedure in the diagnosis of cretinism. I shall explain briefly how this is done.

The osseous development, or "bone age," of the patient is determined by studying the centers of ossification in the x-rays of the patient's bones, and comparing them with Shelton's Tables, which show the normal times of appearance of the various centers.

Slide 3 shows the bones of a cretin of 12 months, who had only those centers of ossification which are normally present at birth. The administration of thyroid during the next 5 months produced an unusually rapid response, causing all the centers which are normally present at 4-5 years, to appear.

Slide 4 shows how we chart the developmental rates and illustrates the usual response of a cretin to *adequate* doses of thyroid. The child's actual age is plotted along the horizontal, the "developmental age" along the vertical. The normal rate of development is represented by the line rising at 45°. The height is expressed in "height age" in order to compare it with the "bone age", as determined by the x-rays, and the "mental age", as determined by the Binet-Simon or Gesell tests. Before treatment the bone age is *always* very markedly retarded, the height is stunted, and the mental age is retarded. Nearly all of our cretins show the type of response to thyroid illustrated by this chart, and we consider that a study of the developmental rates in this way is essential in determining whether or not the dosage of thyroid is adequate. We consider that the treatment is adequate only when the bone age is approaching closer and closer to the normal level. Along with this the height age usually approaches the normal, but frequently the mental age may lag behind, irrespective of the dose.

Slide 5 shows the response to what may be considered an excessive dose.

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Slide 6 shows the effect which an interruption of treatment produces upon the rates of development.

Slide 7 shows the results of inadequate treatment. This illustrates the condition usually encountered in the cretins who come under our observation, after being treated elsewhere with the very small doses of thyroid, which unfortunately have been recommended in the literature in the past. Even with very small doses, the cretin usually loses all obvious signs of hypothyroidism within a few weeks or months, such as the cretinoid facies, the skin and hair changes, the mental torpor, and makes a certain amount of growth. However, he may lag further and further below the normal level of development unless a careful record is kept, and unless sufficient thyroid is given. It seems probable that if just sufficient thyroid is supplied to raise the metabolism to normal levels, the previously stunted hypothyroid child will probably grow and develop at the normal rate, but will not attain the normal levels for his age. In order to accelerate the developmental rate sufficiently to allow the hypothyroid child to make up for his lost years, and to approach his normal age level, it is probably necessary to produce a slight degree of hyperthyroidism. This usually requires a dose of 2 or 3 grains a day, irrespective of age, instead of doses of 1/10 to 1/2 grains, as has been recommended in the past. We usually give sufficient thyroid to keep just below the level of toxic manifestations.

DIAGNOSTIC DIFFICULTIES

I wish to discuss, now, some of the difficulties in the diagnosis of cretinism. The question of the diagnosis of mild borderline types of hypothyroidism is open to much dispute. Of recent years, it has become the custom of many medical men to label as hypothyroid almost every infant who is subnormal or peculiar. If the eyes are widely spaced, or the nose flat—in fact, if the infant is ugly or unusual looking in any way—he may be branded as a cretin. Also the infant who is mentally retarded or defective, or is stunted physically, is often diagnosed a cretin. Since most physicians are aware of the importance of osseous retardation, x-rays of the bones are usually taken; and, if even a slight retardation of the bone development is found, the physician considers that hypothyroidism is proved, and thyroid is enthusiastically prescribed. Often these indiscriminate diagnoses are not justified. The Mongolian idiot should be recognized and differentiated. The hypothyroid infant should show definite stunting in height and marked retardation in bone development. However, I do not believe that these alone establish the diagnosis with certainty. The hypothyroid infant almost always shows some dryness and coarseness of the skin and hair, and a dull, phlegmatic disposition, although these changes may be slight. Practically always, his cheeks and lips have a pale, sallow appearance. The child with bright, ruddy cheeks is not hypothyroid. Finally, and most important, if the patient is hypothyroid, there will be a spectacular improvement when thyroid is given, and a relapse to the previous condition when it is withdrawn. I admit that the diagnosis of cretinism in the very young infant is difficult, in fact, it can rarely be made below 6-9 months. I think that it is most important that the physician be on the alert to recognize the condition, and I do not wish to discourage the use of thyroid in the so-called borderline case, because it is important to begin thyroid as early as possible. I do, however, protest against the indiscriminate diagnosis as a final one. In doubtful cases, the use of thyroid should be regarded as a therapeutic trial, and the diagnosis should be reserved. Later, all thyroid should be withdrawn to determine whether there are evidences of retrogression. It is at this time that the determination of changes in blood cholesterol are of great importance, and I shall discuss them in a minute.

First, let me point out another diagnostic problem. It is that of the child who has previously been treated with thyroid by some other physician for a considerable time, and is now brought to us to check the diagnosis. Such a child may present absolutely none of the stigmata of hypothyroidism and may have attained normal height and bone development. It may be impossible to make a diagnosis except by withdrawing thyroid therapy. When thyroid is discontinued, 4-10 weeks

may elapse before any changes may be obvious. During this time there is usually a fairly rapid gain in weight. Finally, one of the first things that becomes noticeable is a loss of the color in the cheeks and lips, and often a circulatory mottling of the skin. The child becomes less energetic and more phlegmatic. The characteristic dryness and coarseness of the skin and hair may not occur for many weeks or months. The changes in the blood cholesterol during this period, however, are of the greatest help diagnostically. Prior to treatment, the blood cholesterol does not always differentiate the cretin from the normal child. Although the cholesterol may be high in the untreated cretin, we have frequently found values of 200-250 mg., which is within the normal range. However, after a hypothyroid patient has been treated with thyroid for a considerable period, and then the medication discontinued, the blood cholesterol rises very markedly. In the course of 6-13 weeks we usually observe a rise to 350-600 mg., and at times we have seen it go as high as 800-1000. This change does not occur in the non-hypothyroid individual who has previously been treated with thyroid. This is illustrated by Slide 8.

Juvenile Hypothyroidism

The Typical Clinical Picture

There is even more dispute in regard to what constitutes the characteristics of hypothyroidism appearing in later childhood than there is in regard to cretinism which presumably depends upon a congenital thyroid insufficiency. Most childhood endocrinologists agree, however, that many cases present a well defined clinical picture which can be definitely identified as hypothyroid. In these instances, the patient seems to have grown and developed during the first few years of life. Later there is a slowing or stopping of growth and development, so that the child lags further and further behind the normal for his age. The characteristic cretinoid facies does not develop, nor do the myxedematous deposits of the adult usually occur. The child looks much younger than his actual years. He is dwarfed, with skeletal proportions corresponding to his height rather than his age. The body build is stocky or chunky. The patient is overweight, but not markedly obese. The features are somewhat broad and coarse, the expression a little dull. There is always marked delay in the osseous development. The second dentition is delayed, and the teeth are often poorly formed and carious. The mental development is usually somewhat retarded. The cheeks and lips are generally pale. The skin is cool, somewhat dry and roughened; and the hair is dry. However, the skin and hair changes are usually much less marked than in cretinism. Finally, the diagnosis is clinched by the rapid growth and striking changes in the body configuration upon the administration of thyroid.

The Borderline Cases

Although this typical picture of hypothyroid dwarfism can be recognized at a glance by one familiar with it, there are many other cases where the diagnosis is open to dispute. As you know, there are many different types of dwarfs. The slender, symmetrical dwarf, with delicate skin and hair has been described as hypopituitary. Between this slender type and the chunky hypothyroid type I have described, there are innumerable clinical variations. The older endocrinologists attempted to classify some as thyropituitary, others as pituitaro-thyroid. These diagnoses were guesswork, and there was no real proof of either the hypothyroid or hypopituitary factor. In addition to these various dwarfs, there are many children who are a little subnormal mentally, a little stunted physically, or show some abnormality of the skin or hair. Frequently uncritical diagnoses of mild or borderline hypothyroidism are made in such cases.

Diagnostic Methods of Study

How, then, is the diagnosis of hypothyroidism to be made? We do not yet know the absolute criteria of diagnosis, but we wish to discuss some of the methods of study which are available, and to point out some progress which has been made.

1. The *osseous development.* We have pointed out that in cretinism and in proven cases of juvenile hypothyroidism marked retardation of the osseous development always occurs. Some years ago, when this fact be-

came known, some endocrinologists went so far as to assert that the osseous development was controlled *exclusively* by the thyroid gland. Accordingly, they claimed that osseous retardation always signified hypothyroidism and that the only thing necessary in diagnosis was to take an x-ray of the bones. *I do not believe that this is true.* We had hoped that it might be true, and accordingly we studied the rates of growth, osseous development, and mental development of all our dwarfs in the same way that we studied cretins. The studies convinced us that high degrees of osseous retardation may occur in many different types of dwarfs who have nothing suggestive of hypothyroidism either clinically or biochemically, and who do not respond to thyroid medication. (This was illustrated by a number of photographs and charts.)

2. *Epiphyseal dysgenesis*: Although the delay in the time of appearance of the epiphyseal centers of ossification may occur in conditions other than hypothyroidism, there is an abnormality in the structure of these centers which is apparently characteristic of hypothyroidism, and which we have encountered in no other condition. However, its diagnostic value is limited because it usually occurs only in very marked conditions of hypothyroidism. This is a characteristic stippled, mottled or fragmented appearance of the osseous centers which has been called hypothyroid epiphyseal dysgenesis. (Slide)

Since the bone studies are of only limited value, let us see what other methods are available for the study of thyroid function. There are three: (3) *B. M. R.*, (4) *Blood cholesterol*, (5) *The urinary excretion of creatine.*

Unfortunately, it is very difficult to determine the B. M. R. in children, partly because of lack of cooperation, and partly because of the unreliability of normal standards for children, especially when applied to individuals of abnormal body build. The blood cholesterol and urinary creatine can be determined by reliable chemical methods. (The various types of study were illustrated by a number of charts. These studies are still in progress and will be published elsewhere at a later date.) The levels of cholesterol and creatine do not offer a sharp distinction between the *untreated* hypothyroid patient and the normal child. However, we believe that the blood cholesterol, the urinary creatine, and also the B. M. R. (when it can be satisfactorily measured) can be used as yard-sticks to determine the effect of thyroid upon the organism. In attempting to establish methods for the diagnosis of hypothyroidism, we have administered small doses of thyroid to the patients and used these yard-sticks to study the degree of sensitiveness to this dose. We believe that the hypothyroid patient responds sensitively to a small dose of thyroid, and the normal child is much less responsive. In addition to this, we have administered the thyrotropic hormone of the pituitary gland and studied the effect upon the cholesterol, creatine and B. M. R. We believe that a positive response may mean that the thyroid is present and can react to stimulation.

Identical studies are being made on hypothyroid children, on normal children, and on dwarfs presenting no features of hypothyroidism. It is hoped that eventually data will be accumulated which will permit a more accurate diagnosis of hypothyroidism in the borderline conditions. At present the most promising methods of study are (1) the quantitative measurement of sensitivity to thyroid by means of change in the blood cholesterol and the creatine excretion, (2) the study of the response to thyrotropic hormone by the same methods, (3) the changes in the blood cholesterol which occur on withdrawal of thyroid medication.

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DISCUSSION

DR. CHARLES E. WAGNER (Wilmington): I would like to ask Dr. Wilkins how he arrives at a proper dosage in the treatment of these cases of cretinism and hypothyroidism. I would also like to ask him to give us some of the figures on the excretion of creatine in the urine. I couldn't quite see what the figures were on the charts. I am just wondering what those figures are.

I wish to thank Dr. Wilkins very much, personally and on behalf of the society, for com-

ing here to give us this excellent presentation and very thorough discussion today.

DR. JOHN BAKER (Milford): I, too, want to thank Dr. Wilkins for his excellent presentation. My knowledge of endocrinology is rather meager and this discussion today has certainly enlightened me a great deal on hypothyroidism.

In my six years in Delaware I don't believe I have seen one case of sporadic cretinism. I have seen children in whom I tried to make a differential diagnosis to determine whether they had a hypothyroid condition or not. I think the greatest incidence has been in trying to determine whether a child was either a Mongolian idiot or a cretin. In some of these children I have gone so far as to give thyroid therapy. I thought I got some results in one. In the others I couldn't see any benefit at all but the mothers thought they could see something.

I think frequently in the very young children, that is, in the infants from the age of a year to two years, we overlook hypothyroidism because we do not think of it. We are thinking more of rickets and of the effects of malnutrition, whereas, if we would be a little more conscious of the thyroid probably as a growth factor, we would be more alert in looking up these things.

I, too, would like to ask Dr. Wilkins a question. Some authorities state that at the time of puberty as the youngsters change over, at that stage hypothyroidism becomes more frequent. I would like to know if he thinks that is true. I would also like to know what he thinks of the most important signs, picking up thyroid insufficiency in an infant of approximately six or seven months, or if it can be told at that age. Also, if he attempts to do basal metabolic rates on children under three years of age.

In the treatment we get marked response to thyroid therapy in osseous development and in growth, but what does Dr. Wilkins believe or think of the mental changes that we find in these children after giving them that therapy?

I wish to thank him again for his excellent presentation.

DR. CARL H. DAVIS (Wilmington): Dr. Wilkins has taken the child after it is too late to really do more than give palliative treatment. The really important problem, I think, is to look forward to the new generation and work toward preventive treatment.

Those of you who visited deQuervain's clinic in Berne and have seen that array of all types of cretinism, all types of hypothyroidism, and have listened to him explain that the mental changes undoubtedly occur before the seventh month of intrauterine development, know his views on it. He says that in Switzerland there is absolutely no treatment they have been able to devise that will make a normal individual out of the cretinoid infant at birth. They can develop it somewhat physically, yes, but that infant will be greatly retarded mentally and will be a burden to its family and to society all its life. All of you noticed, of course, in the charts that the mental age of all of these cretinoid infants and children as they have developed with thyroid medication remained very much below normal and frequently the curve after a certain period of time leveled out showing that their mentality did not continue to improve.

The plea which I would make is that you treat the women during the period of pregnancy with a view to eliminating the possibility of thyroid deficiency. That means that all women should have ample iodine in their food intake during the entire period of pregnancy, and if the woman is hypothyroid herself she should have ample thyroid medication during the period of pregnancy. There may be other factors necessary but we do know that the woman needs the iodine and we know that the hypothyroid woman needs thyroid if she is to develop a reasonably normal child.

The mere giving of iodine to the entire population at certain cantons in Switzerland has largely eliminated the incidence of congenital goiter. Instead of it being around eighty per cent as it was formerly it is now under twenty per cent in these same cantons. They tell us, though, that at birth they cannot tell whether an infant is going to show the stigmata of hypothyroidism later or not, that

it is usually several months old before they see any of the evidences of this.

I sincerely hope that as Dr. Wilkins works on this problem he will try to bring home to his associates the need of prophylactic treatment of the obstetrical patients in demonstrating these very unfortunate conditions in the youngsters.

DR. WILKINS: I am afraid I have been given material enough for another complete lecture. I will try to be brief.

I am very glad Dr. Davis brought up the obstetrical side of the problem. I certainly agree with his viewpoint of prophylaxis, but I don't know about it. I have a very definite case of cretinism in a nephew of a doctor. The patient's mother had been treated with Lugol's solution during pregnancy. I don't know how to explain that.

I think the problem of endemic cretinism in Switzerland is also a somewhat different one, probably with etiological factors different from our sporadic cretinism.

What Dr. Davis said in regard to the disappointing results in the mental development is true, but the outlook is by no means as hopeless as Dr. Davis implied. We have a number of cretins who are of practically normal mentality. One of these is a charming bright-eyed little girl of six now, who is doing her work in school and is right up to par in every way. She has a lag of only six months. Many cretins do reach a certain mental level and stop. In some cases the results are very disappointing and hopeless. I think in such cases there has been a definite, permanent, organic damage to the nervous system in utero, that cannot be corrected. On the other hand I do feel that during the first two, three or four years of life the results are not hopeless. I don't mean to be too optimistic or enthusiastic about treatment.

Dr. Baker asked, in the first place, whether we determine the basal metabolic rate in children under three. I would say it is quite unsatisfactory in children under six and even in many children over six. That is the reason for making these other studies. I might point out here that these studies are detailed, long drawn out scientific studies. I don't mean to imply that it is necessary or desirable that one should make studies of that type on every case, but we are trying to discard previous ideas and establish certain concrete knowledge and objective facts on hypothyroids, hoping eventually to be able to set up certain criteria for diagnosis.

You asked a question in regard to the signs in the infant under six or seven months. There may be no signs. It is very difficult to diagnose cretinism under that age. If one is suspicious of hypothyroidism in the child of six or seven months, or one year of age, one is perfectly justified in going ahead and treating as a trial, because, as Dr. Davis pointed out, the earlier this treatment is made, whether prenatal or postnatal, the more important it is. But when the child has gone on with treatment for a year or two, stop, and see what happens then; whether there is a retrogression. Or maybe you will want to carry on for two, three or four years, and then stop and follow the cholesterol.

In regard to Mongolian idiocy versus cretinism, that is a mistake that is made not unusually. Of course the Mongolian idiot has certain characteristic features that one usually can recognize, the slant of the eyes, and all the things with which you are familiar. The Mongol very often has normal osseous development, and if you find a normal osseous development, I think you may eliminate hypothyroidism or cretinism entirely.

Another condition that is frequently mistaken by the average practitioner for cretinism is a peculiar wide spacing of the eyes that suggests a cretinoid facies. It is called hypertelorism and is due to an abnormality in the sphenoid bone at the base of the skull. I have seen cases treated for years for cretinism without any improvement, which have proved to be hypertelorism.

Dr. Wagner inquired in regard to the absolute values of creatine in the urine. It varies a great deal. It depends somewhat upon the age and the weight of the child. The normal child usually excretes somewhere between 50 and 150 milligrams per day. In hypothyroidism the creatine may be entirely absent or it may run up as high as normal levels sometimes. The characteristic thing is

the marked increase in creatine output upon the administration of thyroid to the hypothyroid case. Those curves which showed the black going way up represented an increase to as much as four or five hundred milligrams per twenty-four hours.

The question of dosage and treatment in childhood is a very different one from the dosage and treatment in adult life. I agree with Means and other adult endocrinologists in their belief that the adult myxedematous patient should be carried along at as low a metabolic level as is consistent with the clearing up of the physical characteristics, the abnormal skin and hair, and the comfort and good looks of the patient. In other words, if the patient gets along at a level of minus ten, it is better for him than to be brought up to a normal metabolic level. In childhood, we have the entirely different proposition of increasing the developmental rate, not only to the normal rate, but of speeding up the patient to regain his lost years, and to catch up with normal. Therefore we try to give as large a dose of thyroid as the child can tolerate without toxic symptoms. That dose is usually one and a half to three grains of U. S. P. thyroid daily. When toxic symptoms in the way of diarrhea or cramps or very excessive nervousness, or very continued and excessive loss of weight occur, the dose is decreased. But we don't hesitate to push the dose to the point of slight symptoms of hyperthyroidism.

CLINICAL ALLERGY*

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When your President honored me with the invitation to address you, I told him I would gladly accept provided that I would be allowed simply to speak to you and not read a paper.

I want to go over with you some of the high spots of the fundamental principles of allergy as we now know them. In the first place, it must be admitted that we know nothing of the underlying causes of allergy. Many theories have been proposed: Endocrine dysfunction, autonomic nervous inbalance, disordered carbohydrate metabolism, and many others. Yet not one of these theories has stood the test of critical examination. But one thing we do know: that the allergic individual has an inherited defect, something that has come down to him from his ancestors, and that defect is that he can become sensitized to things in his environment far more easily than can normal individuals.

This means, above all, from the practical standpoint that an individual's sensitivity pattern is not a fixed and static affair. It means that new sensitivities can arise and old ones go by the board. It means that this tissue can lose its sensitivity and another get one. It means that symptom pictures will change and that there will be relapses and renewals of symptoms.

The things to which people become sensitive are determined by various factors, notably the intensity of their exposure to certain things and the circumstances under which they are exposed to those things. For example, ragweed pollen is the commonest pollen in this country, and consequently ragweed hayfever is the commonest form of pollinosis. Women become sensitized far more often to the orris root with which they powder their noses than do men. We spend one-third of our lives in bed and consequently sensitivity to the materials of which bedding is made is exceedingly common. In infancy the foods which are oftenest eaten, egg, milk and wheat, are the ones which most frequently will be found to give positive tests in youngsters.

Sensitization is more readily accomplished when the effectiveness of the skin or mucosal barrier is reduced by inflammation or trauma. So bronchial infection (e. g., whooping cough) often opens the way for asthma, while hayfever often follows an operation on the nose or throat in the pollen season.

Sensitization takes place by way of a body surface, as a rule, skin or mucous membrane. Since that substance to which we become sensitized must be in solution it is obvious then that the dry skin offers a fairly good barrier to sensitization, and sensitization doesn't often take place by way of the skin. However, it

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can. For example, in many occupations an individual is exposed to damp substances; so the baker often becomes sensitive to the wheat of the dough which he kneads. Or it may be simply the moisture of perspiration as, for example, in the summertime when there is enough perspiration to dissolve enough nickel out of the white gold of a wrist watch or the frames of glasses to sensitize certain individuals to nickel, and produce a local dermatitis.

The digestive tract, with its moist surface and with its fluid contents, offers a much more common and obvious route for sensitization. Yet here, too, the body has a certain amount of protection. In the first place, the substances which we put into that digestive tract are often enough denatured. Cooking takes care of that. It is, therefore, significant that we find sensitivity in adult life very often to those foods which are eaten in a raw state. Again, digestive juices may sufficiently denature proteins so that we don't as readily become sensitized by that route.

In that connection it is perhaps significant that food sensitivity is not only rather frequent in infancy when hydrochloric acid is not yet present, but again in later years, when many lose their gastric free hydrochloric acid and become sensitized to things ingested, notably drugs. The most common among these are the catharties, especially phenolphthalein.

However, when we come to the respiratory tract the stage is best set for the induction of sensitization, in that we have a moist surface, a surface that has no digestive ferments to protect it in the slightest, that has contact, not with cooked, but always with native proteins. And so sensitivity occurs commonest by way of the respiratory tract and we find the severest forms of sensitivity in that group of cases.

The clinical manifestations of hypersensitiveness are so numerous that I could take the next hour simply mentioning diseases in which sensitivity has been suggested as a possible cause. It is rather amusing, as I look back on the days when as a youngster I dared to lift my voice in a staff meeting and suggest that asthma might be due to sensitivity to feathers or dust and got nothing but raised eyebrows and shrugs of the shoulder. Now all kinds of patients with everything, from falling of the hair to falling of the arches, are sent to the allergy clinic with the thought that perhaps sensitivity might be the cause. Certain it is that from what was apparently a narrow field this matter of sensitivity has branched out until it touches practically every phase of clinical endeavor.

I will just touch some of the high spots in the clinical manifestations of allergy. For example, in the respiratory tract. Hayfever, obviously, yes, but less obviously vasomotor rhinitis, allergic rhinitis, that thing which is perennially present because the contact with the substance to which the patient is sensitive is perennially present.

That may be often overlooked. Why? Because many times it is so mild as not to excite the patient's suspicion. The fellow who sneezes six times in a row doesn't think he is sick, and yet the normal individual is entitled to only one, two, or at most three consecutive sneezes. If he sneezes six times in a row he is as allergic as the severest asthmatic. Again: it is overlooked because the late results of such chronic allergic rhinitis—the sinus disease, the advanced polyposis of the mucous membrane—dominate the picture. Polyposis itself we feel is a rather strong, in fact, a practically certain indication of the presence of an underlying sensitivity.

In the lower respiratory tract asthma is the outstanding example. But there are other and milder forms. So, for example, it doesn't have to go on to the matter of broncho-spasm with actual dyspnea, but there may be involvement simply in the trachea and larger bronchi so that the patient suffers from paroxysms of an unproductive cough, his "bronichal trouble," or his "cigarette cough," as he calls it, that he has gotten used to and pays no attention to. Or it may involve the mucous membrane of his larynx so that a transient edema coming and going without rhyme or reason gives him a transient but frequently recurring hoarseness.

In the gastrointestinal tract there are conditions that have been at times—please underline the "at times"; it doesn't happen always—traceable to hypersensitiveness. We will begin at the beginning. Aphthous stomatitis,

in some instances, particularly those with recurring crops of these ulcers can be due to sensitivity. Further along in the stomach you can have the mildest kind of a symptom in the way of slight indigestion, or there may be the violent convulsive spasm of the stomach that results in the prompt vomiting of the egg, to which the child happens to be sensitive, the minute he gets it into the stomach. Or there may be more drawn-out chronic affairs suggestive of pylorospasm. In a certain number of cases frank peptic ulcer of the stomach or of the duodenum may be due to allergy. Again I plead with you, don't quote me as saying that duodenal ulcer is due to allergy. It isn't in the overwhelming majority of instances. But in a very definite minority it is due to that. Be particularly on your guard to think of it in those patients who have been subjected to repeated surgical procedures and who still continue to get the ulcers. You can cut out an ulcer but you can't cut out the sensitivity.

Farther along in the digestive tract food sensitivity can give rise to diarrhea or, at times, to constipation, depending on whether the element of spasm or of hyperperistalsis is predominant. In the large bowel mucous colitis is, at times, and I think quite often, due to food sensitivity. A fifth of the cases of pruritus ani have been found to be due to food sensitivity.

In the skin, urticaria usually and eczema commonly is on an allergic basis. In the course of fungus infections of the skin, such as trichophytosis between the toes, a person of allergic strain can become sensitive to the fungus protein and break out in a generalized rash called dermatophytid. Purpura is occasionally the result of sensitivity.

In the urinary tract, bladder pain, bladder spasm, and in children nocturnal enuresis (again, not all of them, just a small percentage) may be allergic in origin. In such allergic cases you won't get anywhere with your measures of treatment until you find the underlying sensitivity. Renal colic, even hematuria, maybe so caused at times. Well, why not? Because in the skin you can have not only eczema and urticaria, but you can also have purpura on the basis of certain food allergies; and if you can have allergic purpura in the skin, you can have it in the urinary mucosa. Such cases may simulate renal tumor or renal tuberculosis. I have seen at least four kidneys that had been removed from individuals on the suspicion of renal tumor because of recurrent hematuria, yet when those kidneys were removed they were as normal as I hope both mine are this very minute. I remember one case particularly in which the stage was set for nephrectomy. She had unilateral hematuria and unilateral colic to go with it. On the day that the operation was to take place, she had a pain and colic on the other side, and since they couldn't take out both kidneys for suspected tumor they left them both in. The woman herself made the diagnosis when she found out some months later that when she ate enough strawberries she would have, not just an itchy rash, but actual hematuria and colic, which was invariably unilateral.

In the nervous system, there is notably migraine. There are so many other causes of headaches, though, that you can't be dogmatic or cite figures. However, think of allergy as a possibility in the causation of headaches for which other causes have not been found.

Perhaps once in a hundred epileptics—unfortunately the percentage isn't larger—the epilepsy has been found to be due to sensitivity. Tobacco sensitivity is perhaps the most common that has been discovered in this connection.

In the cardiovascular system, allergic manifestations are uncommon, except the well known condition of angioneurotic edema. There is one condition, however, in which a third of the cases are on an allergic basis, and that is paroxysmal auricular tachycardia.

In the eyes, allergy may manifest itself not only as vernal conjunctivitis but occasionally as episcleritis and corneal ulcer. Occasionally the pain of migraine may be limited entirely to the orbit.

From the standpoint of the blood, malignant neutropenia has been shown to be caused by sensitivity to certain drugs. Purpura, with or without thrombocytopenia, may occasionally be on an allergic basis. Here again,

drugs, insulin, and foods are among the commoner causes.

I could go on and cite yet other types of sensitivity, but the time is short, so I will hasten on to certain principles of prophylaxis, diagnosis, and treatment.

PROPHYLAXIS

We are just beginning to realize the possibilities in regard to prophylaxis, the prevention of the development of sensitization in these sensitizable individuals. The keynote of the whole situation is: moderation in all things, not to have excessive exposure to things which we know are good sensitizers, not to overeat, or eat too often of the same type of food, not to go into occupations in which there is bound to be exposure to many sensitizing substances. Yet one of my hayfever patients thought it would be a fine thing to take up chicken farming. He got a feather asthma for his pains.

Use kapok or cotton bedding rather than animal epidermal substances, namely, feathers or hair. The allergic child or the child of allergic parents shouldn't have animal pets.

Patients should not have operations of election on the upper respiratory tract during the pollen season. About five per cent of all cases of hayfever as we see them will give you the history that their hayfever began in the year in which somebody did a submucous resection, or a tonsil and adenoid operation during a pollen season. If you don't remember another single thing I tell you today, that one thing will have been worth the price of admission: Not to subject your patients of allergic heredity to operations of election on the respiratory tract during the pollen season.

DIAGNOSIS

The first axiom in the diagnosis of allergic states is not only the awareness that allergy exists, but the knowledge that it is extremely common. Fifteen per cent of all of us are definitely allergic and remain so all our lives, and all our illnesses throughout our lives will be colored by that allergic strain, which can crop up in many different guises from the cradle to the grave.

The next point to remember in diagnosis is that some allergies of course obviously suggest themselves in this day or generation. When a patient comes to you and tells you he has sneezing from the 15th of August to frost, why, that is ragweed sensitivity. You don't have any hesitancy in diagnosing sensitivity there. But when a patient tells you that he has had indigestion off and on irregularly and you examine him from one end to the other and get nothing in the way of positive clinical and x-ray findings, and all your laboratory data are negative, and still his troubes continue, then you ought at least to get suspicious about allergy as a possible factor. If then you question him and you find that, oh, yes, he has other complaints that he never bothered to tell you about because he has lived with them so long, namely, sneezing a dozen times every morning when he gets up, or you uncover the fact that he had eczema for two years in infancy (a fact that you didn't dig out of him in the first place as you should have), or if you then find further as you climb around on his family tree that it is hanging full of allergic forebears, well, then, you have struck the most important means in spotting the unusual, the hidden allergies: namely, the questioning of every patient routinely about allergic diseases in himself or his family. It is far more useful to find out something about his relatives' illnesses such as asthma, hayfever, hives, eczema or migraine, than to put down useless information as to what they died of.

Here again, of course, family histories will be gotten far more accurately if you get them from women members of the family. A man will remember whether his uncle Henry was hung for being a horsethief, but that is about all. It takes a woman to know that Grandmother's Sister Susan got hives every time she ate an artichoke.

A diagnosis to be of use in allergic disease must be complete. The commonest cause for failure in the management of allergic disease is the failure to get a complete diagnosis, complete in that it shall find out all the substances to which the patient is sensitive, not just a half dozen—complete in that it shall work out not just the allergic side of his troubles but the rest of his difficulties, particularly with regard to complications as they so often occur in the respiratory tract where, if an allergy

lasts long enough and particularly if it is perennial, that is, lasts all the way around the calendar, sinus complications are invariably bound to occur. Then you have infection on top of allergy and you can't cure one without adequately handling the other.

TREATMENT

When it comes to treatment here again the watchword is thoroughness, completeness of following up all your therapeutic leads. You can't do things as you do them in so many other types of treatment. An arthritic, for example, is looked over for foci of infection. You find diseased tonsils and a few abscessed teeth and a questionable prostate, and possibly stones in the gall bladder. Well, you don't that minute subject that patient to the removal of all those things at one fell swoop. No. You flip a nickel, or figure out that probably the teeth are the most likely causes of trouble; at least that is where he seems to have most of his focal infection. You pull the teeth out and see if he gets better as a result of that. If he doesn't, then you go ahead with the tonsils, and so on, seriatim.

In allergy, you can't just cut out the wheat and see whether the patient gets better on that alone, and then if he doesn't get better, try something else. Yet that is what patients are constantly doing. Thus, you ask him, "What do you sleep on?" "Feathers, but I used a kapok pillow for apout three months and wasn't a bit better, so I chucked the kapok pillow, as it was hard and uncomfortable, and went back to feathers."

His experience doesn't necessarily mean that he wasn't sensitive to feathers. He was sensitive to a half dozen other things and simply getting rid of the feathers did no good. But you don't do any permanent good unless you get rid of the feathers and the other five things, too. If you only break out half the teeth of a buzz saw the remaining teeth will still bite you every time they come around.

The next axiom in the treatment of allergic disease is this: avoidance of that to which the patient is sensitive gives by far the best results. If a patient has ragweed hayfever and gets away from where there is ragweed pollen he will be completely relieved of symptoms. If a patient gets asthma only from feathers and he changes from feathers to kapok bedding, he will be completely relieved of his asthma. But you must see to it that such avoidance is scrupulously carried out. Yet, for example, how often does treatment fail, because, even though the patient has changed from feathers to kapok, his roommate in the next bed, or even in the same bed, still sleeps on feathers.

If a patient is sensitive to eggs then you have to cut out not just the obvious egg in the diet, but the egg in all of its hidden forms. And when you start looking into the many things in which egg is used you are appalled at the list.

Not every patient, in fact not one in a thousand hayfever sufferers, can take a trip to Europe in the ragweed season. All the rest of them have to face the music at home. Under those circumstances there is still something to be accomplished by attempts in the direction of partial avoidance. A simple pollen filter put in the window will give the patient a comfortable night. If he can't even afford that, keeping the bedroom windows closed all day long when the air is full of pollen, keeping the bed covered all day long with a cover of some impervious material such as glazed chintz or paper, removed carefully at night, that keeps the pollen from sifting on the pillow, will help give the patient a better night.

But if complete or partial avoidances, so far as they are carried out, aren't completely successful, then you have to proceed to the procedures called desentization. I won't go into the details of that sort of thing. There are many ramifications. I will simply pick on the commonest type that is used by the general practitioner, hayfever treatment, and will point out a few of the high spots in the way of errors that are responsible for most of the failures in that procedure.

In the first place, you must treat a patient to every pollen to which he is sensitive. If a patient is treated with grasses only and he happens to be sensitive to grass and plantain, too, you won't get a perfect result.

The next point is that you must suit the dosage to the case. You can't treat all patients by the same scheme of dosage. Yet that is exactly what the directions accompany-

ing the circular that the manufacturers put out with their pollen extract do. No two people are sensitive in exactly the same degree. Consequently, the dosage varies from patient to patient. One fellow may require twenty times as much as the next fellow in the way of pollen extract to give him protection. The one thing that the manufacturer has to see to is that the dosage which he recommends is safe, that it shall not cause serious reactions in the very sensitive, and consequently it is geared down to their level. Hence, in many, many instances it proves wholly inadequate.

Moreover, your pollen treatment should not stop, that is, the maximum dose should not be reached until just before the season opens. Yet, how often does a mother come to the doctor and say, "Doctor, will you please finish Johnnie's ragweed treatment by July 1? He goes away to camp and there is nobody there to give him his injections." If the doctor does it, then by the 15th of August Johnnie's tolerance for ragweed has again dropped practically to the vanishing point and he has a lousy season of it. Moreover, once the season has arrived you should continue giving injections, but at a much lower level.

These, then, are the high spots as I see it in the matter of treatment. My time is up. Now I must crave your indulgence for not staying with you the rest of the day, since I have to try to catch the Matapeake ferry for Annapolis at twelve o'clock. (I don't see how I can do it.)

I thank you very much.

University Hospital.

DISCUSSION

PRESIDENT PRICKETT: I am sorry Dr. Kern is in such a hurry, but he has to speak in Washington this afternoon and then he has an hour and twenty minutes to catch his boat. I outlined his route for him as far as Matapeake. I hope he makes it. I certainly want to thank Dr. Kern for his excellent paper. I am sure we have all benefited by it.

DR. WILLIAM MARSHALL (Milford): I think that Dr. Kern gave a most excellent talk. He went down into the minute phases of something that is very important and affects a very large proportion of the cases we see as general practitioners. I think some of the doctors have argued that of the patients as they come in to our offices as high as one out of every seven will show some sign of allergy, and I don't think that is a very high percentage. The Doctor just mentioned fifteen per cent a little while ago. Even if that percentage is true, still that makes a tremendous lot of thought for us to give to the science of allergy. It is a new work, and this consideration of the hypersensitivity along with allergy and anaphylaxis makes for a study that is more or less inexact. I don't know when we ever will be able to get to the real cause of these things. They involve so much of the blood chemistry and the vital processes of life that we probably will never know some of it, but if we know something about the cure, as the Doctor has just given it to us, I think we shall have obtained a tremendous amount from his talk this morning.

I enjoyed it very much and I thought it was one of the most complete papers on allergy and hypersensitivity that I had ever heard.

PRINCIPLES INVOLVED IN THE DIAGNOSIS AND TREATMENT OF ALLERGY*

With Discussion of Hayfever

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Philadelphia, Pa.

The importance of an appreciation of the subject of allergy has assumed increasing proportion. Its various symptom-complexes have been found to ramify into all branches of medicine, until it has been incumbent upon every physician and specialist to familiarize himself with the principles involved in its diagnosis and treatment.

A better understanding of the subject will be had, if cognizance is taken of one fundamental factor: namely, that of heredity.

By virtue of the hereditary factor we may assume to have an individual who is born without clinical manifestation; but by means of a constitutional predisposition, inherits the capacity to become sensitized when sufficient contact with the offending substance has occured. This capacity to become sensitized is localized in a group of sensitive cells, termed

*Read before the Kent County Medical Society, Dover, May 3, 1939.

the shock tissues or organs by Coca. The shock tissue in hayfever is the nasal mucous membrane; in bronchial asthma, it is the bronchial mucous membrane; and in urticaria and eczema, it is the skin.

When the offending substance, called the antigen or allergen, comes into contact with the antibody, termed the reagin, which is present in or upon the cells and in the circulating blood, an allergic reaction ensues, with the liberation of a histamine-like substance from the cell, which is responsible for the symptoms.

The allergen or antigen involved, reaches the shock tissue by the hematogenous route. It must therefore be a water-soluble substance. To demonstrate this hypersensitivity by means of the skin test, the allergen must be brought into contact with the vessel wall by going through the epidermis. This is accomplished either by the scratch or intracutaneous method.

The reagins can also be demonstrated in the serum of atopic individuals by the methods of passive transfer of Prausnitz and Kustner. This method furnishes proof of the allergic mechanism involved—an interaction between the allergen and reagin, with the production of a positive reaction in a sensitized, non-allergic individual.

Inheritance determines not only the incidence of allergy, but also governs the age at which the allergic manfestations may make their appearance. Observers have shown that the age of onset of allergic conditions is dependent upon the degree of inheritance. It is therefore assumed that the greater the antecedent family history for allergy, the earlier the onset of the allergic state. This in the majority of cases is true. Heredity also seems to influence the clinical type or hypersensitiveness by determining which shock organ is to be involved.

However, heredity in itself is not sufficient to produce symptoms. A second important factor is also necessary—that of contact. For without contact, an individual with a predisposed constitution may never develop symptoms. This is best illustrated by taking an individual subject to the fall type of hayfever, who develops hayfever each year about the middle of August when exposed to the ragweed pollen. This same individual when vacationing in Europe fails to develop symptoms during the ragweed season. The reason for this is that although constitutionally predisposed, the all important factor of adequate contact is absent.

We may now concern ourselves with the immunologic approach in the diagnosis of the allergic state. It consists of:

1. A detailed history and physical examination.
2. Allergic skin testing.
3. Clinical or therapeutic trial.

A complete and detailed history is of prime importance. A carefully recorded history may not only aid in establishing the diagnosis but also aid in uncovering the etiologic factor. For example, with a history of recurrent seasonal attacks of sneezing, rhinorrhea, nasal blockage, and itching of the nose, eyes and soft palate, occuring in the fall, from mid-August to the first frost, a clinical diagnosis of ragweed hayfever is easily made. An etiologic diagnosis is also made from the history if the pollinating season is known to the historian.

Of further aid will be an atopic personal or family history for allergy. This may not be obtained in all cases under study.

The social history in allergic cases plays a most important part. Under this heading will be found the occupation of the individual, the foods which the patient may be clinically sensitive to, and the type of bedding the subject uses. The environmental factors are important, as they may produce symptoms. The effect of animal contact is noted, as well as the effect of dust, wind, effort, tobacco, and emotional upsets upon the symptoms of the individual patient.

The diagnosis of the allergic state having been made, skin tests are then resorted to in an attempt to determine the specific offending substance. There has been considerable discussion as to whether the scratch or intracutaneous methods of testing are preferable. Opinions vary with the individual student. The scratch method is often used and if found negative the intradermal method is then resorted to. Both methods have their advan-

tages. We, personally, prefer the intradermal method and use it for testing both infants and adults. In infants, however, the concentration of the extract is diluted. The intradermal method of testing is more accurate and sensitive than the scratch technic, and reactions are obtained which would otherwise be missed if the scratch technic were to be used. The intradermal method may produce a few false positive reactions and occasionally constitutional reactions. These rarely occur in competent hands, and are usually the result of using too concentrated an extract.

The reactions that are produced by the intradermal skin tests are read in ten minutes, and recorded as marked, moderate, slight, doubtful and negative, depending upon the size of the wheal and the surrounding erythema. The reactivity of the skin of different patients varies and note of this should be made in the interpretation of all reactions.

It must be realized that a positive skin reaction is only an index of cutaneous sensitivity and may bear no relationship to the clinical sensitivity of the patient. At other times the skin may fail to react, although the patient is clinically sensitive. These negative skin reactions are due to an absence of the skin-sensitizing reagins. These reagins, however, may be present in the mucous membrane of the eye, nose, bronchi, or gastro-intestinal tract. Hence, the eye and nasal test, as well as trial and elimination diets are resorted to, with those allergens which are suspected through the history.

The principles employed in the treatment of allergy are (1) elimination or avoidance of the offending substances from the diet and environment of the patient and (2) desensitization.

I have in a very sketchy manner introduced to you the subject of allergy as related to the methods in the diagnosis and treatment.

This is not a symposium on allergy. I have been asked, however, to speak to you specifically on the subject of hayfever.

There are two distinct types of hayfever—the seasonal and the perennial. We will concern ourselves with the seasonal type.

Seasonal hayfever may be divided into three distinct types:

1. Early spring—due to the pollens of the trees, and extending from the middle of March to the early part of June.
2. Late spring or early summer—due to the pollens of the grasses, and extending from the early part of May to the middle or end of July.
3. Late summer or early fall—due to the pollens of the weeds, and extending from the middle of August to the first frost.

The trees are responsible for less than 1 per cent of the cases of hayfever; the grasses for approximately 35 per cent; and the weeds for 65 per cent of the cases.

The trees commonly tested for will depend upon the locality the patient resides in. The most important trees are oak, birch, maple, poplar, and sycamore. The most important grass pollen is timothy, and the most important weed is ragweed and occasionally plantain.

The average uncomplicated hayfever case presents no diagnostic difficulties. A careful detailed history almost always establishes the clinical diagnosis. Knowing the principal pollens, together with the dates of onset and subsidence, a specific or etiological diagnosis can be made. In addition it must be ascertained whether the patient is hypersensitive to other allergens, either in his environment or in the foods ingested.

The clinical and etiological diagnosis of hayfever is next corroborated by the demonstration of positive skin reactions to the pollens responsible for the patient's symptoms. The value of the intradermal method of skin testing over the scratch technic will at once become apparent. The scratch technic permits only a positive or negative reaction. The intradermal method, by employing varying concentrations of the pollen ascertains the relative degree of sensitivity of the patient to the particular pollen in question, and in doing so, acts as a rough guide in the treatment of the patient.

The extracts that are used routinely in practice are based on the nitrogen content, i.e. mg. of total nitrogen per c.c. Four dilutions of the extract are prepared, in increasing multiples of ten, so that for routine testing and

treatment there are four vials of 0.0001, 0.001, 0.01, and 0.1 mg. of nitrogen perce.

In testing a patient, therefore, as a general rule, the tests are first made with the 0.0001, 0.001, and 0.01 strengths. The 0.1 dilution is only used in testing those cases that give a slight or moderate reaction to the weaker dilutions. The tests are performed by the intradermal method.

Treatment of the patient is started with that dilution which barely gives a positive reaction. As a general rule, treatment is instituted, by injecting subcutaneously, 0.1 cc of 0.001 mg. total nitrogen. The amount is then increased until the patient is receiving 1.0 cc. Subsequent doses are gradually increased, always staying within the level of tolerance, (as designated by the absence of a marked local or constitutional reaction) until the patient is receiving 1.0 cc of the highest dilution or 0.1 mg. total nitrogen per cc. The maximum amount of pollen extract should be administered before the onset of the hayfever season.

METHODS OF TREATMENT

Three methods of treatment have been devised in the treatment of hayfever: (1) the coseasonal or phylactic, (2) the preseasonal and (3) the perennial method. The selection of the particular method will depend upon the physician, the patient, and the time of year.

The coseasonal or phylactic method of desensitization is employed in that group of patients who present themselves to the physician just prior to the season or after the symptoms of hayfever have begun. Treatment in this type of case must be given very cautiously. Small frequent doses are given subcutaneously or intradermally. Because of the prevalence of pollen in the atmosphere at the time the patient is receiving treatment the dose must be kept low. Because of the tendency to marked local and constitutional reactions, it must be used most cautiously and in competent hands. Treatment is usually efficacious when started during the season, although better results are obtained with the preseasonal and perennial methods of treatment.

The preseasonal method of desensitization is the method most commonly employed. The principle of this method is to increase the dosage of the pollen extract until the point of a maximum tolerance of the patient is reached, which should be before the onset of the pollinating season. The injections are administrated subcutaneously, at intervals of three-seven days, and in gradually increasing doses according to the reactions and tolerance of the patient. With the onset of the season, the dose is diminished to approximately 25-30 per cent of the maximum, and at the height of the season it is diminished to 50 per cent of the maximum dose and then continued at that level, at weekly intervals throughout the remainder of the season. The decrease in dose is to correct once again for the concentration of the pollen in the atmosphere at the time the patient is under treatment.

The necessity for individualization in treatment cannot be too strongly stressed. No set increase in dose can be formulated for any individual patient. The physician should be guided by the local reaction of the patient at all times, and rarely will a constitutional reaction result.

We prefer the perennial methods of treatment. Its advantages over the preseasonal method have been corroborated by many observers. The perennial method attempts to retain the tolerance of the patient rather than build it up each season. Instead of discontinuing treatment at the end of each season, treatment is continued post-seasonally once a week until the maximum dose is once more established. The interval is then lengthened to two-four weeks, and treatment is continued at the maximum level until the onset of the next hayfever season when the dose is again decreased as outlined in the preseasonal method.

The advantages of the perennial method are many. It serves to maintain the tolerance of the patient at a constant level. The results are as good as by other methods and it offers more hope of a permanent remission of symptoms. It maintains contact between the patient and physician throughout the entire year. It is possible to begin treatment at any time of the year. It allows for vacations and periods of illness. It lessens the number of visits the patient has to make to the physician. The only objection that has been raised

against the perennial method has been the occrences of constitutional reactions. We have found constitutional reactions to occur rather infrequently and as frequently as in the other methods of treatment. If the few precautions, as outlined above, are taken into consideration, there need be no fear of such reactions. In the final analysis, the consensus of opinion indicates that the perennial method of treatment offers the best results.

The results of pollen therapy are very favorable. Satisfactory results are obtained in the majority of cases, with relief of symptoms as great as 90 per cent. Results are more easily obtained in cases of hayfever due to the trees and grasses, than in the type due to the weeds. This is probably due to the longer season in the latter type, and the greater concentration of the pollen in the atmosphere.

Failures to obtain results will depend upon the development of new sensitivities, to the pollens, inhalants or foods. Other reasons for failure in treatment may be due to (1) incorrect diagnosis, (2) impotent extracts, (3) insufficient number of injections, (4) inability of patient to develop sufficient tolerance, (5) and failure to avoid or eliminate test-positive allergens from the diet and environment.

The prognosis in an uncomplicated case of hayfever is favorable. Knowing the role that heredity plays in this dissease, cures are not likely to occur. The excellent relief obtained each year, is of a temporary character, and treatment must be continued for an indefinite period of time.

SUMMARY

The methods and principles involved in the diagnosis and treatment of allergy have been presented. The importance of heredity as a predisposing factor in the development of allergy has been stressed.

The principle involved in the diagnosis of allergy is the determination of the specific allergen responsible for the patient's symptoms. This is accomplished by the three methods used in the diagnosis: (1) a detailed history and physical examination, (2) skin tests, and (3) the method of clinical or therapeutic trial.

The principles and methods employed in the treatment of allergy have been presented. They consist of (1) the elimination or avoidance of all test positive allergens from the diet and environment of the patient, and (2) hyposensitization.

The treatment of hayfever has been briefly discussed. The three methods in common use are described. The results and prognosis have been indicated.

57th and Sansom Streets.

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Buie, L. A.: Practical Proctology. Philadelphia, Saunders, 1937, 512 p.

Jackson, C. and Jackson, C. L.: Diseases of the Air and Food Passages of Foreign-body Origin. Philadelphia, Saunders, 1936, 333 p. and appendix 636 p.

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Schwarz, J. C. (editor): Who's Who Among Physicians and Surgeons, Vol. 1, 1938. N. Y., 1938, 1336 p.

EDITORIAL

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DELAWARE DISAPPROVES

On May 17th last, at the St. Louis meeting of the A. M. A., their House of Delegates unanimously voted its opposition to the so-called Wagner Health Bill (U. S. S. 1620), introduced February 28, 1939, and now in committee. An analysis of the Bill as it now reads will be found in the *Journal of the A. M. A.*, for June 3, 1939, page 2296, together with a summary of some 22 points which briefly indicates the official position of organized medicine, and the reasons therefore. It is our understanding that the Senate Committee, as well as Senator Wagner, was much impressed with the facts and arguments presented at the hearing by the representatives of the A. M. A., and it is quite likely that the Bill will be amended considerably before it comes to the floor for a vote. It is our personal belief that it will not come to a vote at the present session of Congress.

At a special meeting of the House of Delegates of the Medical Society of Delaware, held in Wilmington June 7th last, a resolution was adopted unanimously condemning the present Wagner Bill, and a copy of said resolution was ordered sent to each of our representatives in Congress, urging them to oppose the Bill. We have every right to expect that the fairness and common sense of our Congressmen will prompt them to act, when the time comes, in accordance with our wishes. To further this end, the profession stands ready to furnish them with any further information they may desire.

The A. M. A. summary referred to above follows:

SUMMARY

1. The Wagner Health Bill does not recognize either the spirit or the text of the resolutions adopted by the House of Delegates of the American Medical Association in September, 1938.
2. The House of Delegates cannot approve the methods by which the objectives of the National Health Program are to be obtained.
3. The Wagner Health Bill does not safeguard in any way the continued existence of the private practitioners who have always brought to the people the benefits of scientific research and treatment.
4. The Wagner Health Bill does not provide for the use of the thousands of vacant beds now available in hundreds of church and community general hospitals.
5. This Bill proposes to make Federal aid for medical care the rule rather than the exception.
6. The Wagner Health Bill does not recognize the need for suitable food, sanitary housing and the improvement of other

environmental conditions necessary to the continuous prevention of disease.

7. The Wagner Health Bill insidiously promotes the development of a complete system of tax supported governmental medical care.
8. While the Wagner Health Bill provides compensation for loss of wages during illness, it also proposes to provide complete medical service in addition to such compensation.
9. The Wagner Health Bill provides for supreme Federal control; Federal agents are given authority to disapprove plans proposed by the individual states.
10. The Wagner Health Bill prescribes no method for determining the nature and extent of the needs for preventive and other medical services for which it proposes allotments of funds.
11. The Wagner Health Bill is inconsistent with the fundamental principles of medical care established by scientific medical experience and is therefore contrary to the best interests of the American people.
12. The fortunate health conditions which prevail in the United States cannot be disassociated from the prevailing standards and methods of medical practice.
13. No other profession and no other group have done more for the improvement of public health, the prevention of disease and the care of the sick than have the medical profession and the American Medical Association.
14. The American Medical Association would fail in its public trust if it neglected to express itself unmistakably and emphatically regarding any threat to the national health and well being. It must, therefore, speaking with professional competence, oppose the Wagner Health Bill.
15. The House of Delegates would urge the development of a mechanism for meeting the needs for expansion of preventive medical services, extension of medical care for the indigent and the medically indigent, with local determination of needs and local control of administration, within the philosophy of the American form of government and without damage to the quality of medical service.
16. The fundamental question is how and when a state should be given financial aid by the Federal government out of the resources of the states as a whole, pooled in the Federal Treasury.
17. The bizarre thinking which evolved the system of Federal subsidies — sometimes called "grants-in-aid"—is used to induce states to carry on activities suggested frequently in the first instance by officers and employees of the Federal government.
18. The use of Federal subsidies to accomplish such Federally determined activities has invariably involved Federal control.
19. Any state in actual need for the prevention of disease, the promotion of health and the care of the sick should be able to obtain such aid in a medical emergency without stimulating every other state to seek and to accept similar aid, and thus to have imposed on it the burden of Federal control.
20. The mechanism by which this end is to be accomplished, whether through a Federal agency to which any state in need of Federal financial assistance can apply, or through a new agency created for this purpose or through responsible officers of existing Federal agencies, must be developed by the Executive and the Congress, who are charged with these duties.
21. Such a method would afford to every state an agency to which it might apply for Federal assistance without involving every other state in the Union or the entire government in the transaction.
22. Such a method would not disturb permanently the American concept of democratic government.

Similar resolutions have also been adopted by the Woman's Auxiliary of the Delaware Society, thus making the disapproval unanimous.

A New Dietary Factor

About three years ago Day, Langston and others of the University of Arkansas, placed monkeys on a presumably adequate diet containing all known vitamins. This diet consisted of a mixture of casein, polished rice, ground whole wheat, cod liver oil, ascorbic acid, salt mixture and sodium chloride. All monkeys fed this diet developed anemia, leukopenia, gingivitis, diarrhea, anorexia and loss of weight. Death invariably occurred in from one to three months. These investigators then tested the effects of the addition of nicotinic acid to their routine deficiency diet. The nicotinic acid had no demonstrable effect on the pellagra-like oral lesions in these animals. In later tests the Arkansas physiologists found that 1 mg. of riboflavin added to the daily diet will not prevent the development of pellagra in monkeys, nor will a combination of nicotinic acid, riboflavin and thiamin appreciably affect the course of this deficiency disease. If the daily deficiency diet is supplemented by 10 Gm. of dried brewers' yeast, however, or by 2 Gm. of liver extract, normal body growth and a normal blood picture are maintained over long periods. They conclude from these results that monkeys require some factor contained in yeast or in liver extract in addition to the factors commonly recognized as a part of the vitamin B complex. For this unknown nutritional factor they tentatively suggest the name "vitamin M." Attempts to isolate and identify the new antipellagra "vitamin" are now in progress in their labortory.

—(*J. A. M. A.*, April 1, 1939, p. 1258)

"Vitamin K," a Principle Useful in Certain Hemorrhagic Conditions

The Cooperative Committee on Vitamins, representing a combined committee of the Council on Pharmacy and Chemistry and the Council on Foods of the American Medical Association, considered the evidence for a principle called "vitamin K," reported to be useful in the treatment of certain hemorrhagic conditions. The committee recommended that a preliminary report be issued on this principle and the recommendation was adopted by the Council on Pharmacy and Chemistry. Dr. A. M. Snell of the Mayo Foundation, who has been working with this principle, prepared a report which was adopted by the Council for publication. The Council agrees with Dr. Snell that the principle known as vitamin K appears to have therapeutic usefulness in the hemorrhagic manifestations of hepatic and biliary disease. The Council has authorized its Committee on Nomenclature to study the question of a suitable non-proprietary name which shall not be therapeutically suggestive. The Council voted also to consider with view of acceptance brands of "vitamin K" under strictly limited claims for usefulness in the hemorrhagic diathesis of hepatic and biliary disease.

—(*J. A. M. A.*, April 15, 1939, p. 1457)

BOOK REVIEWS

Life and Letters of Dr. William Beaumont. By Jesse Q. Myer, M. D., late Associate in Medicine, Washington University. Pp. 327, with 64 illustrations. Cloth. Price, $5.00. St. Louis: C. V. Mosby Company, 1939.

This Life of Beaumont, America's pioneer physiologist, and one of the truly great characters in medical history, is a reprint of the original of 1912, and is especially welcome because it contains several hitherto unpublished letters written by his famous patient, Alexis St. Martin. In addition to containing the original introduction by Sir William Oser, there is "A Present Day Appreciation of Beaumont's Experiments on Alexis St. Martin," by Dr. Andrew C. Ivy, Professor of Physiology and Pharmacology, Northwestern University, which is most illuminating. The Illustrations are very interesting, and are climaxed with Dean Cornwell's 1938 painting in oil of Beaumont collecting a specimen of gastric juice from St. Martin's stomach.

The text itself is scholarly and exhaustive, yet most readable, and as the story of the great Army researcher, working on his fistulous patient at an isolated army post, unfolds one is fascinated. Here is the life story of a really great medical man, and it should be read by all whose scientific spirits can still be stimulated and inspired through biography.

Alcoholics Anonymous. Pp. 400. Cloth. Price, $3.50. New York: Works Publishing Company, 1939.

This is the interesting biographical tale of over 100 chronic alcoholics who were considered hopeless, but who for the past four years have been cured through the ancient and honorable means of religions. The psychological approach is good—through contact with a previously reformed drunkard; then the moral approach is carefully made, on a nonsectarian basis; finally, the patient who really wants to be cured sells himself on the idea of a spiritual regeneration. Many cases require hospitalization, etc., the details of which are up to the physician. In suitable cases, this book for laymen may be productive of a great amount of good.

Synopsis of Clinical Laboratory Methods. By W. E. Bray, M. D., Professor of Clinical Pathology, University of Virginia. 2nd edition. Pp. 408, with 68 illustrations. Cloth. Price, $4.50. St. Louis: C. V. Mosby Company, 1938.

In this edition the author continues his purpose of producing an up-to-date reference manual of clinical laboratory procedures. Fourteen new procedures of accepted value have been added since the first edition. Unnecessary details are omitted. The book admirably fulfills its purpose.

What It Means to Be a Doctor. By Dwight Anderson. Pp. 96. Cloth, $1.00. Paper cover, 25 cents. New York: Public Relations Bureau, Medical Society of the State of New York, 1939.

This little brochure tells the public what it means—to doctors generally, to doctors individually, and especially to the public, who will find here interesting data on the doctor and his education, skill, mode of thought and life, and his character. Most important, it includes concise and accurate information on the organization of medicine, with a generous hint of its present-day economic and legislative problems. This is a clever combination of information and propaganda—put it on your reception room reading table.